ORAL CANCER BACKGROUND PAPERS

Chapter I: Descriptive Epidemiology

Working Draft

A. State of the Science

Definition of Oral/Pharyngeal Cancer

Cancers of the oral cavity and pharynx account for 3% of all cancers in the United States. Oral cancer usually includes cancer of the lip, tongue, salivary glands, and other sites in the mouth; while pharyngeal cancer includes cancers of the nasopharynx, oropharynx, and hypopharynx. More than 90% of oral or pharyngeal cancers are squamous cell in origin.

For classification purposes, oral and pharyngeal cancers sometimes are grouped with laryngeal and esophageal cancers, with which they share etiologic features. However, in these background papers, they will not be. Furthermore, oral cancer will be defined to include cancers of the lip, tongue, other mouth sites, and the oropharynx. Cancers of the salivary gland, nasopharynx, and hypopharynx will not be included, as they account for less than 10% of all oral cancers and are etiologically and biologically distinct. Sarcomas will also not be discussed for similar reasons.

Epidemiologic Measures and Data Sources

Incidence, mortality, and survival are the primary measures for assessing the impact of cancer in population groups. *Incidence* is the frequency of new cancer cases during a defined period of time, generally expressed as the rate per 100,000 persons per year; the *mortality rate* is the frequency of cancer deaths per 100,000 persons per year. The *observed survival rate* is the proportion of persons with cancer who survive for a specified period of time after diagnosis, usually 5 years. This statistic is often presented as a relative survival rate, in which survival from cancer is corrected for the likelihood of dying from other causes.

Data for describing the patterns of oral cancer come from two main sources, mortality data derived from death certificates and cancer registries. The National Center for Health Statistics (NCHS), within the Centers for Disease Control and Prevention (CDC), collects and analyzes death certificate data from all 50 states and is the main source of U.S. mortality statistics. These data permit assessment of the incidence, survival, and mortality rates for different segments of the population (defined by age, sex, race/ethnicity, or other characteristics).

Cancer registries attempt to include all cancer cases among residents of a defined geographical area. Data collection involves checking all possible sources of cases—hospitals, pathology laboratories, physicians' offices, and death records. A number of registries exist in the United States and Puerto Rico. In fiscal year 1994, 37 states received support from CDC for cancer registries: 25 to enhance established registries and 9 to develop registries where none existed. These state-based programs of cancer surveillance, authorized by Congress in 1992, will provide the basis for appropriate policy decisions and allocation of scarce program resources.

The National Cancer Institute (NCI) collects data from nine cancer registries (5 states and 4 metropolitan areas) as part of its Surveillance, Epidemiology, and End Results (SEER) program. Although they are not nationally representative in the statistical sense, the SEER sites were selected for their epidemiologically significant population subgroups and account for about 14% of the U.S. population. For the past 20 years, SEER data have represented the primary source for statistics on national incidence and survival.

Incidence and Mortality Data

Based on 1991 SEER data, the overall incidence and mortality rates for oral and pharyngeal cancer combined are 10.4 per 100,000 population and 2.9 per 100,000 population, respectively. The annual incidence of 15.7 per 100,000 for males far exceeds the rate of 6.0 per 100,000 for females.[1]

Mortality rates show similar differentials: 4.5 per 100,000 per year for males, 1.7 per 100,000 per year for females. This gender difference is also evident in the lifetime risks of developing oral cancer: 1.5% for males and 0.7% for females (based on 1989-91 incidence rates).

Black males in the United States have an incidence rate of oral cancers about one-third higher than their white counterparts (20.7 versus 15.3 per 100,000 annually) but more than twice the mortality rate (8.9 deaths versus 4.1 deaths per 100,000). In contrast, black women have an incidence rate (6.2 per 100,000) that is similar to that of white women (5.9 per 100,000), although the difference in mortality rates between these groups is more substantial (2.4 versus 1.6 per 100,000).

Geographic variations in mortality have been noted. For the period 1987-1991, states with the highest mortality rates were: Alaska (4.1 per 100,000), Delaware (4.1 per 100,000), South Carolina (4.0 per 100,000), and Louisiana (3.7 per 100,000). The District of Columbia had a mortality rate more than twice the total national rate (6.8 versus 3.0 per 100,000). Arkansas, Idaho, Wyoming, South Dakota, and Utah had the lowest rates (2.2, 2.1, 1.8, 1.7, and 1.3 per 100,000, respectively). From the 1950s through the 1970s, the Southeast had high mortality rates, but these have since decreased.

Trends over time in oral cancer incidence are very different for different subgroups of the population. From 1973 to 1991, the oral cancer incidence rate climbed from 16.8 to 20.7 per 100,000 persons per year among black men, but declined slightly for white men from 17.5 to 15.3 per 100,000. Among women, incidence rates remained relatively constant at about 6.2 per 100,000.

Persons with oral cancer often have multiple primary lesions, and have up to a 20-fold increased risk of having a second oral cancer. Persons with primary tumors of the oral cavity and pharynx also are more likely to develop cancers of the esophagus, larynx, lung, and stomach.[2-5]

Differences exist by anatomical site as well. Within the oral cavity and pharynx, 29% of cancers involve the tongue and another 17% the lip. Among pharyngeal sites, the oropharynx is the most common site for tumors (39%), followed by the hypopharynx (32%).[6]

Survival

Five-Year Relative Survival Rates

Based on data from 1983-1990, the overall 5-year survival rate for oral cancer was 52.5%. Females fared somewhat better than males (58% versus 50%). Blacks did far worse than whites; only 34% of blacks survived 5 years after the initial diagnosis, compared with 55% of whites. There was a great difference within the black subgroup, however, as the survival rate for black males was only 28%, versus 47% for black females. Overall, the percentage of persons surviving 5 years after the initial diagnosis of oral cancer had not changed appreciably since the 1974-1976 time period.

For cases diagnosed in 1981-1986, the 5-year survival rate for pharyngeal cancers (33%) was slightly more than half that for cancers of the oral cavity (60%). Survival by specific anatomic site ranged from a low of 23% for unspecified or ill-defined sites in the pharynx to a high of 91% for lip cancer. There were significant racial differences for most of the specific anatomic sites, with blacks having poorer survival in each instance.[6]

Five-Year Relative Survival by Historical Stage at Diagnosis

Stage at diagnosis refers to the extent of disease at diagnosis. There are three stages: localized, regional, and distant metastasis. Five-year relative survival rates vary with the stage at diagnosis; localized cancers have the highest survival rates and cancers with distant metastasis the lowest. At diagnosis of oral cancer, most individuals have localized or regional disease: 37%, localized; 43%, regional; 10%, distant; and 10%, unstaged. Five-year survival rates for all oral cancer cases are 79% for those with localized disease, 42% for regional disease, and 19% for disease with distant metastases.[1]

There appear to be no major differences by sex for the distribution of stages at time of diagnosis; however, women with regional and more advanced disease have greater survival rates than do men.[1]

B. Emerging Trends

Incidence Trends

In a review of SEER data from 1973 to 1985, Silverman and Gorsky[7] found that more than 95% of oral cancers occurred in persons older than 40, with a median age at diagnosis of 63 years. As the over-65 population in the U.S. now exceeds 30 million people (about 13% of the population) and has

been the fastest-growing segment of the population in the past decade, further increases in the incidence of oral cancer can be expected.

Significant changes in the racial and ethnic composition of the U.S. population also are anticipated in coming decades. The proportion of blacks in the population (now about 13%) is expected to increase; blacks have historically borne disproportionately high burdens of oral cancer. Hispanic and Asian populations are expected to increase proportionately at even higher rates. Unfortunately, SEER data do not adequately document cancer incidence in these two groups, but the recent addition of two new SEER sites in California and CDC support for state-based cancer surveillance should provide improved data for future analysis.

Changes in risk behaviors, including tobacco and alcohol use, are also likely to have considerable impact on cancer incidence. The Surgeon General's 1964 report on smoking noted that 42% of Americans smoked; today, the figure is about 27%.[8] Alcohol use has also declined, though not as dramatically as smoking.[9] Yet, there has been no commensurate decline in oral cancer incidence during the past 30 years, other than a relatively small decrease in white males. The lengthy lag time between exposure and disease occurrence no doubt explains some of this discrepancy, as does the reality that many factors other than tobacco and alcohol use contribute to development of cancers of the oral cavity and pharynx.

Prediction of incidence trends must also consider the use of tobacco products by the young. As smoking has declined, smokeless tobacco use by young males has increased,[10] particularly in some regions of the country. The 1986-1987 National Institute for Dental Research (NIDR) Survey of Oral Health in Schoolchildren found that 16% of males in grades 6-12 reported current or past use of smokeless tobacco products[11] and almost 39% of current users of snuff products had detectable oral lesions.[12] A preliminary analysis of SEER data for white males under age 30 found that, between 1950 and 1982, the mortality rate doubled.[13] SEER data show substantial increases in incidence and mortality rates for tongue cancer in young males since 1973.

Changes in the intake of protective nutrients (e.g., in fresh fruits and vegetables and dietary supplements) could potentially affect cancer incidence rates in the future.[14,15] (See Chapter III for additional discussion.)

Mortality and Survival Trends

All the factors affecting incidence presumably would affect mortality rates as well; however, some factors influence mortality and survival but not incidence. Among these factors are stage at diagnosis, access to treatment, and the success of treatment.

Unfortunately, the SEER data show no evidence of a significant improvement since 1973 in the

proportion of oral cancer cases diagnosed at earlier (more localized) stages. This disappointing information suggests that efforts at early detection have either not been widely applied or have been inappropriately targeted.

Somewhat more encouraging is that mortality rates have been observed to decline modestly since 1973, even though there was no significant change in incidence or survival rates over the same period.[16] Although potential explanations for this apparent discrepancy have been offered (e.g., improved access to care through Medicare, improved treatment methods, a real decline in incidence masked by improved detection), the data do not permit such conclusions. Surprisingly, the improvement in mortality was not accompanied by a similar improvement in 5-year survival rates, which would have been expected if improved treatment had been responsible for the reduced mortality rates. This apparent inconsistency might be partly explained by the fact that much of the decline in overall mortality comes from a substantial decrease in incidence of lip cancer, which has the highest 5-year survival rate (90%) among oral sites—leaving a residual base of cancer sites with poorer survival times.

C. Opportunities and Barriers to Progress

The National Health Interview Survey (NHIS) has traditionally been a valuable source of data on cancer risk behaviors; the 1990 Health Promotion and Disease Prevention Supplement included questions on public knowledge of oral cancer symptoms and risk factors.[17] The NHIS presents as an opportunity to develop a broader science base on the knowledge, attitudes, and behaviors of the public regarding cancers of the oral cavity. A long-term strategy for expanding use of the NHIS to include selected research objectives in this area might aid initiatives in oral cancer considerably.

The lack of national prevalence data on premalignant lesions has been a significant barrier to understanding fully the occurrence and development of oral cancers. The third NCHS National Health and Nutrition Examination Survey (NHANES III) has attempted to address this concern by including evaluations of oral soft tissues in the oral examination process. These evaluations are based on visual criteria alone and do not entail routine histologic confirmation of findings, but they will still be important as they will be used to develop the first national estimates of the prevalence of such conditions in U.S. adults. Understanding of the significance of premalignant lesions would be further advanced by studies that include longitudinal follow-up to observe malignant transformation. Combined with sociodemographic and behavioral data, such information could help to identify factors associated with malignant outcomes.

Despite the generally high quality of existing epidemiologic data from the sources previously described, there are significant gaps in the science base, including limitations in the coverage of minority populations. However, SEER has attempted to select geographic sites at least partly on the

basis of minority coverage. For example, 10 predominantly black rural counties in Georgia were added in 1978 and American Indians in Arizona were added in 1980 (the Commonwealth of Puerto Rico was a participating site until 1989). In 1992, coverage of Hispanic populations was expanded by adding two new sites in California.

There is substantial evidence that there are racial or ethnic differences in oral cancer beyond the black/white differences noted in publications using the SEER data. An elevated incidence of cancers of the nasopharynx has been reported in persons of Chinese ancestry in the United States and elsewhere;[15] decreased incidence of oral cancers has been observed in American Native populations compared with American whites;[18] and the incidence and mortality rates of oral cancers in Puerto Rico in 1983-1987 were substantially greater than those in the combined U.S. SEER sites for the same time period.[17] A 1981 SEER monograph reported incidence rates for Hawaiian ethnic groups, Hispanics, and American Indians from selected registries,[19] but this material is now dated. It seems likely that CDC's National Program of Cancer Registries will make available more complete, timely, and standardized data on oral cancer by age, race, ethnicity, and geographic region since this program permits participating states to enhance existing data collection or establish new registries.
In addition to more extensive information about demographic risk factors, more information is needed about the reasons for demographic differences in cancer incidence and mortality. Devesa et al. analyzed mortality trends for oral, esophageal, and laryngeal cancers in the United States from 1950 to 1984 and explored trends in tobacco use, alcohol consumption, and nutritional factors as possible explanations for some of the marked race and sex differences.[20] Their finding that only in non-white males did mortality trends tend to parallel the trends for smoking suggests that demographic differences may be important. Goldberg et al. examined mortality trends from 1973-1987 and concluded that the disparity in mortality between males and females was due mainly to differences in incidence, whereas the disparity between races was more likely attributable to differences in survival.[16] Other investigations of this type should be encouraged, as should studies of the reasons for differences in cancer rates between geographic regions.

Incidence of oral cancer among women rose nearly 50% from the late 1940s to 1983-1984 but has remained relatively stable since then. The increase has been attributed to changes in the patterns of smoking and alcohol use among women in recent decades, but nutritional and other factors may have also played a major role.[21]

One of the populations potentially at high risk for several forms of cancer, some of which may present in the oral cavity, is the group of immunocompromised persons infected with HIV. Although the SEER program does not collect data on HIV seropositivity, Kleinman et al.[6] reported a significant increase in the national SEER incidence of oral Kaposi's sarcoma and non-Hodgkin's lymphoma from 1981 to 1987—a period of time coinciding with the developing HIV epidemic in the United States. In addition, Swango et al.[22] reported that the incidence of oral cancer in 1989 was 12-14 times greater among 20-54-year-old males in the San Francisco/Oakland area, among whom HIV is relatively common, than in the other SEER sites combined (see Chapter III).

A variety of behavioral factors are also associated with increased risk for oral cancers. The best known are alcohol and tobacco use[22,23] and environmental risk factors such as exposure to sunlight (for lip cancer).[11,12] However, only alcohol and tobacco use are periodically monitored on a national level. The CDC's Office on Smoking and Health is the primary federal agency charged with routine surveillance of tobacco use. This office uses the NHIS as a key component of its efforts; that survey also collects information on alcohol use periodically. In addition, each year the CDC collects state-specific data on tobacco and alcohol use through the Behavioral Risk Factor Surveillance System (BRFSS). However, although NHIS and BRFSS data help to document current use patterns and trends, they are not particularly valuable in establishing associations between use patterns and cancer incidence.

There are also behavioral factors associated with decreased risk of oral cancer, most notably the consumption of certain nutrients. Accurately tying trends in cancer incidence to changes in risk or protective behaviors would require national databases that target specific age groups, account for the multiple interactions between behavioral and demographic risk factors, and factor in the considerable lag time between exposure to risk or protective factors and the eventual occurrence of disease.

Glossary

age-adjusted rate – a weighted average of age-specific cancer incidence or mortality rates, in which the weights are the proportions of persons in the corresponding age groups of a standard population. Using this rate permits comparisons across populations with dissimilar age distributions.

age-specific rate – the unadjusted rate for a specific age group.

incidence rate – the number of new cancers of a specific type or anatomic site occurring in a specified population during a year, expressed as the number of cancers per 100,000 people.

mortality rate – the number of deaths occurring in a specified population during a year, expressed as the number of cancers deaths per 100,000 people. For this report, only deaths for which oral or pharyngeal cancer was the underlying cause of death are included in the definition.

observed survival rate – the proportion of cancer patients surviving for a specified period of time after diagnosis.

relative survival rate – the likelihood that persons will not die from causes *directly associated with their cancer* at some specified time after diagnosis. It is calculated by adjusting the observed survival rate to remove the effect of death from non-cancer causes. The 5-year relative survival rate is commonly used as an indicator of cancer survival.

stage at diagnosis – the extent of disease at the time it is diagnosed. There are three stages: localized, regional, and distant metastases. Localized cancers have the highest survival rates, and cancers with distant metastases the lowest.

[Terms and definitions adapted from *Cancers of the Oral Cavity and Pharynx: A Statistics Review Monograph, 1973-1987.*[6]]

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